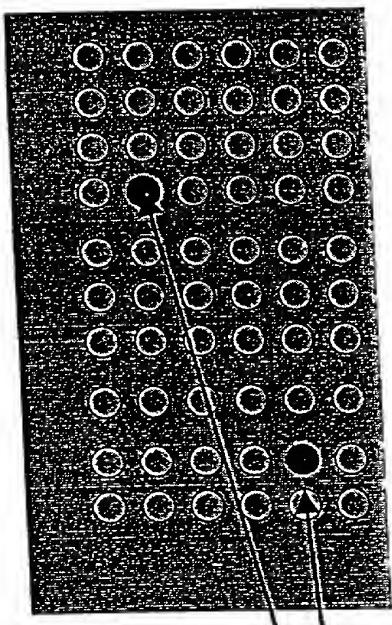


FIGURE 1



Library of Bioactive
Compounds

Library of Target ID
Compounds

Use corresponding
activity-based probe to
identify the biological target

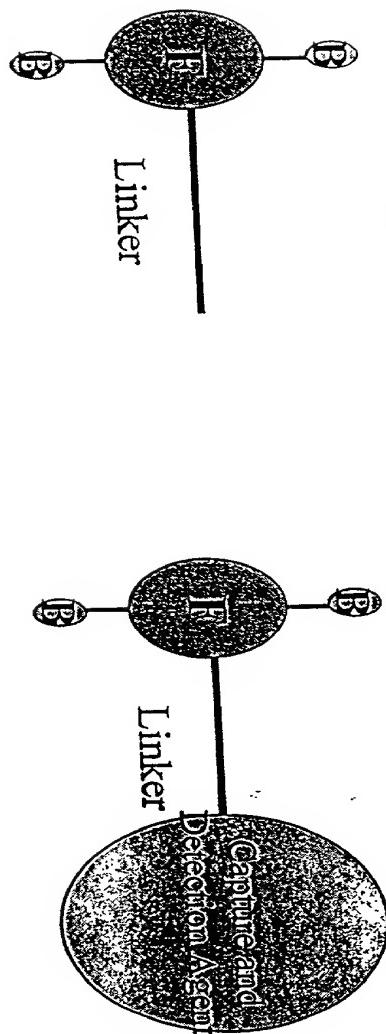
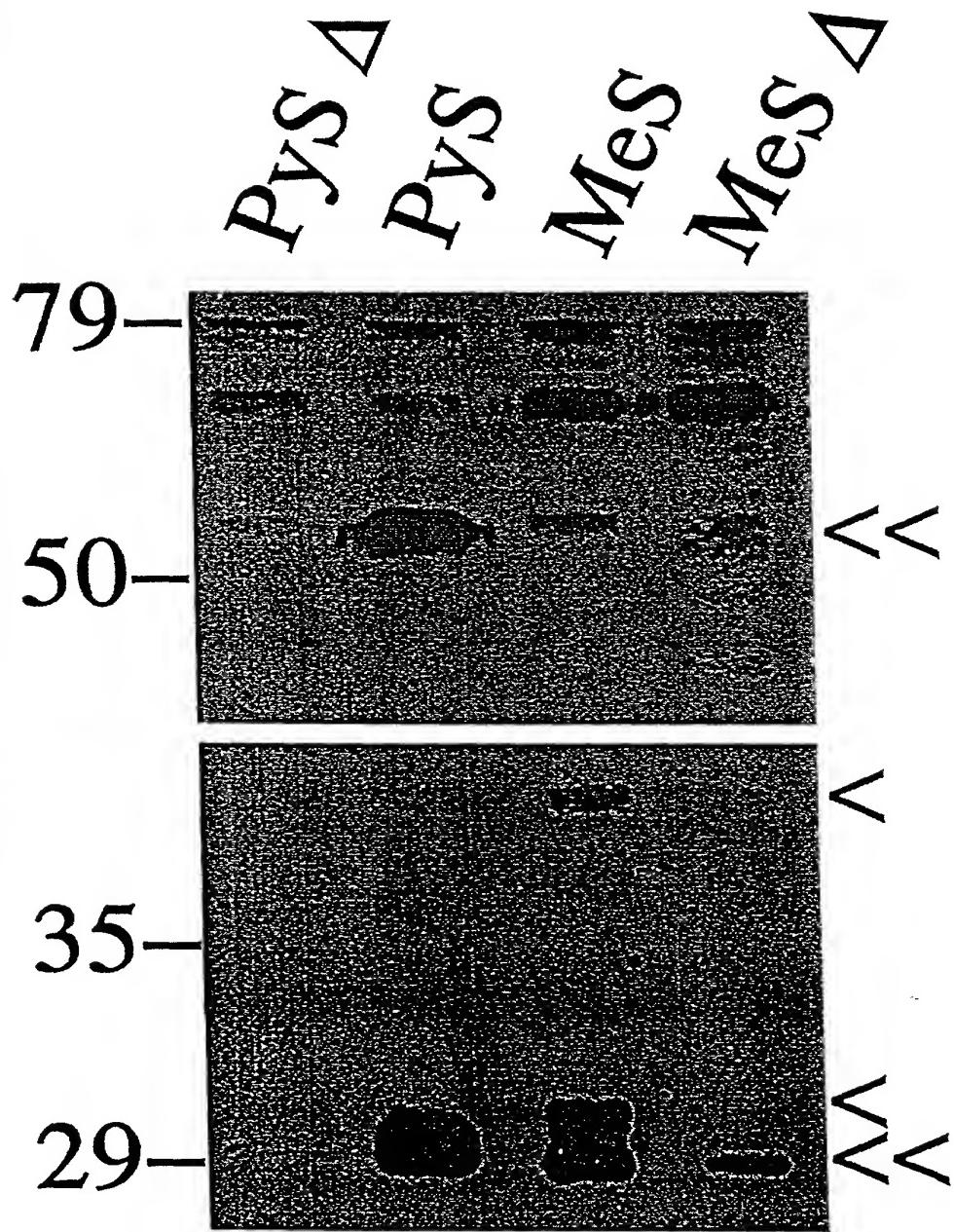
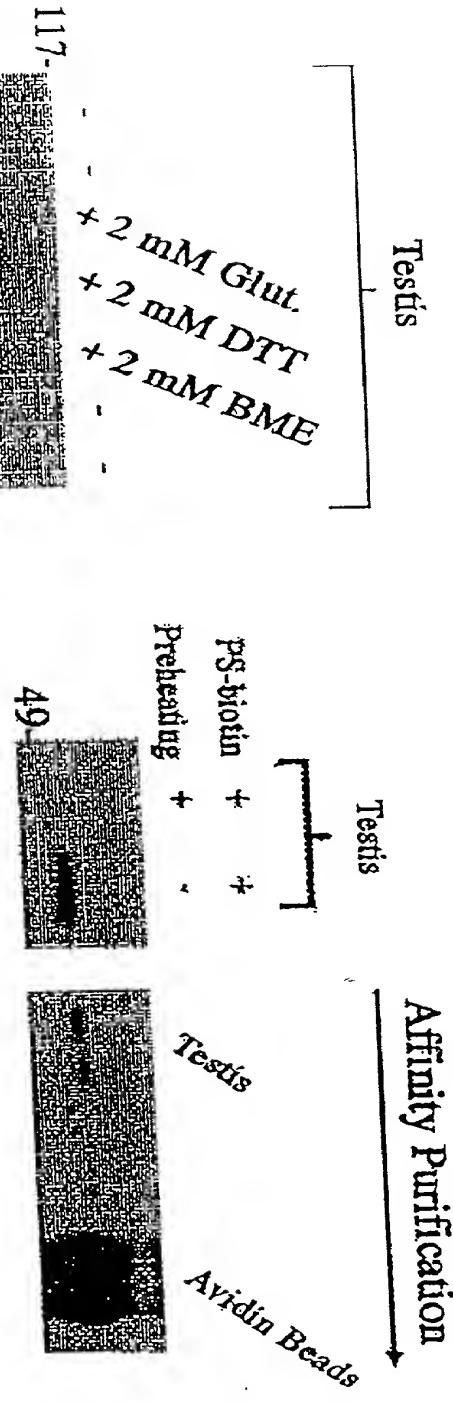


FIGURE 2



Non-Directed Tagged Library of Sulfonates Identifies Probe for ADH Superfamily of Enzymes

FIGURE 3

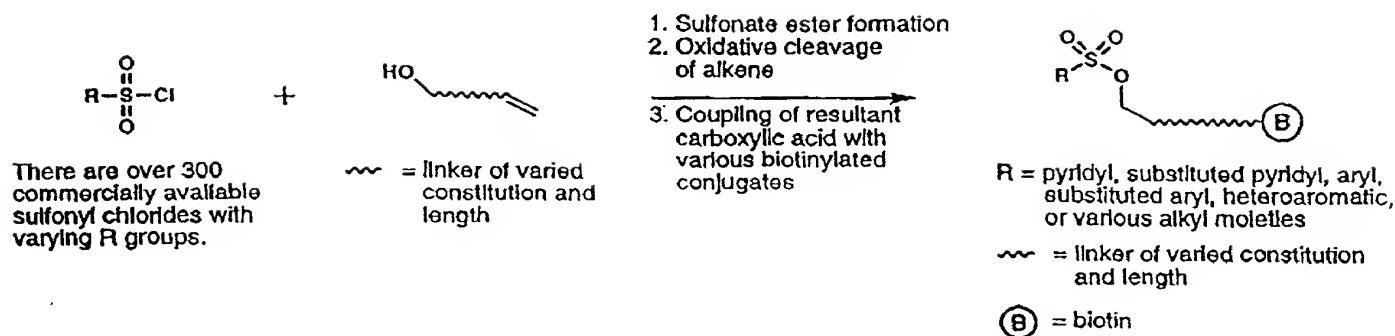


- MALDI mapping identifies tagged protein as aldehyde dehydrogenase (ADH, cytosolic class II)

- 34.
- 29.
- PS-biotin + + + + + + +
Preheating + - - - - - +

alcohol and chemotherapeutic agents

FIGURE 4



There are over 300 commercially available sulfonyl chlorides with varying R groups.

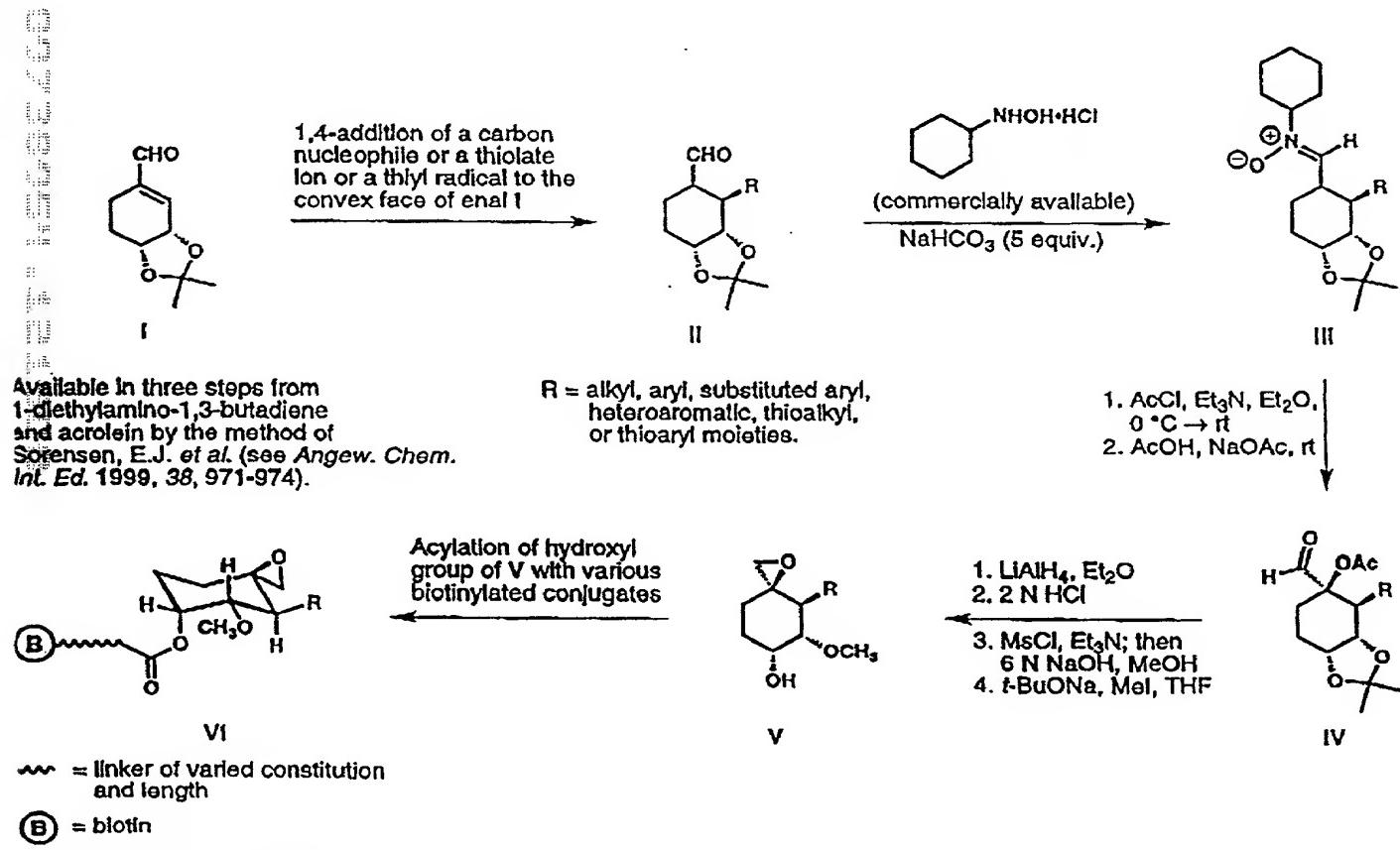
$\sim\sim$ = linker of varied constitution and length

R = pyridyl, substituted pyridyl, aryl, substituted aryl, heteroaromatic, or various alkyl moieties

$\sim\sim$ = linker of varied constitution and length

(B) = biotin

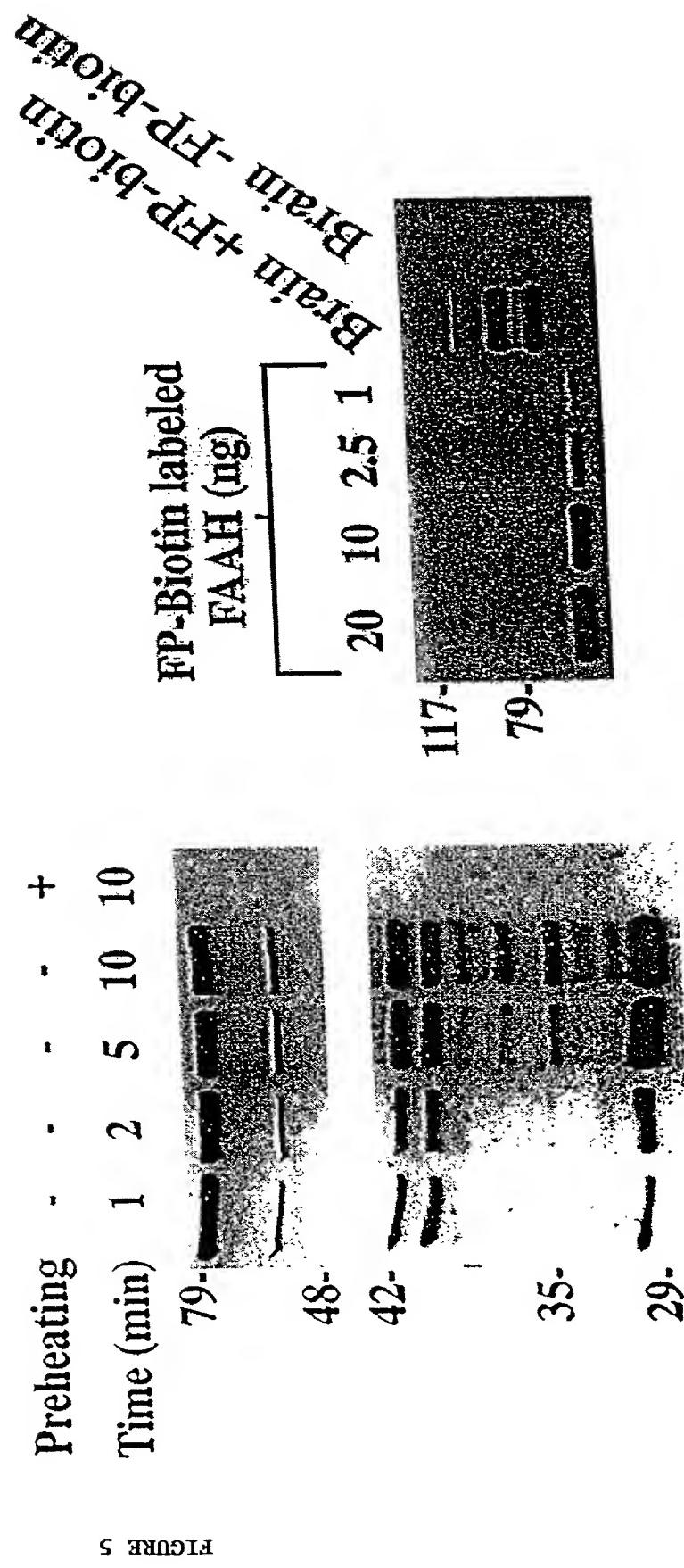
Scheme 1. A pathway for syntheses of various biotinylated sulfonate esters for use in activity-based proteomics studies.



Scheme 2. A strategy for convergent, stereocontrolled syntheses of conformationally well-defined spiroepoxides of type VI. Literature precedent for I → II → III → IV → V can be found in Sorensen, E.J. et al. *Angew. Chem. Int. Ed.* 1999, 38, 971-974. Compounds of type VI are analogs of the metalloprotease (MetAp-2) inhibitor fumagillin and will be employed as covalent affinity agents in activity-based proteomics studies.

FP-Biotin: a kinetic reporter of SH Activity

- The rates at which the majority of SHs react with FP-biotin can be experimentally followed
 - FP-biotin readily detects low femtomole quantities of SHs directly in complex cell/tissue proteomes



Utility of Multiplexed probes in identifying Serine Hydrolases

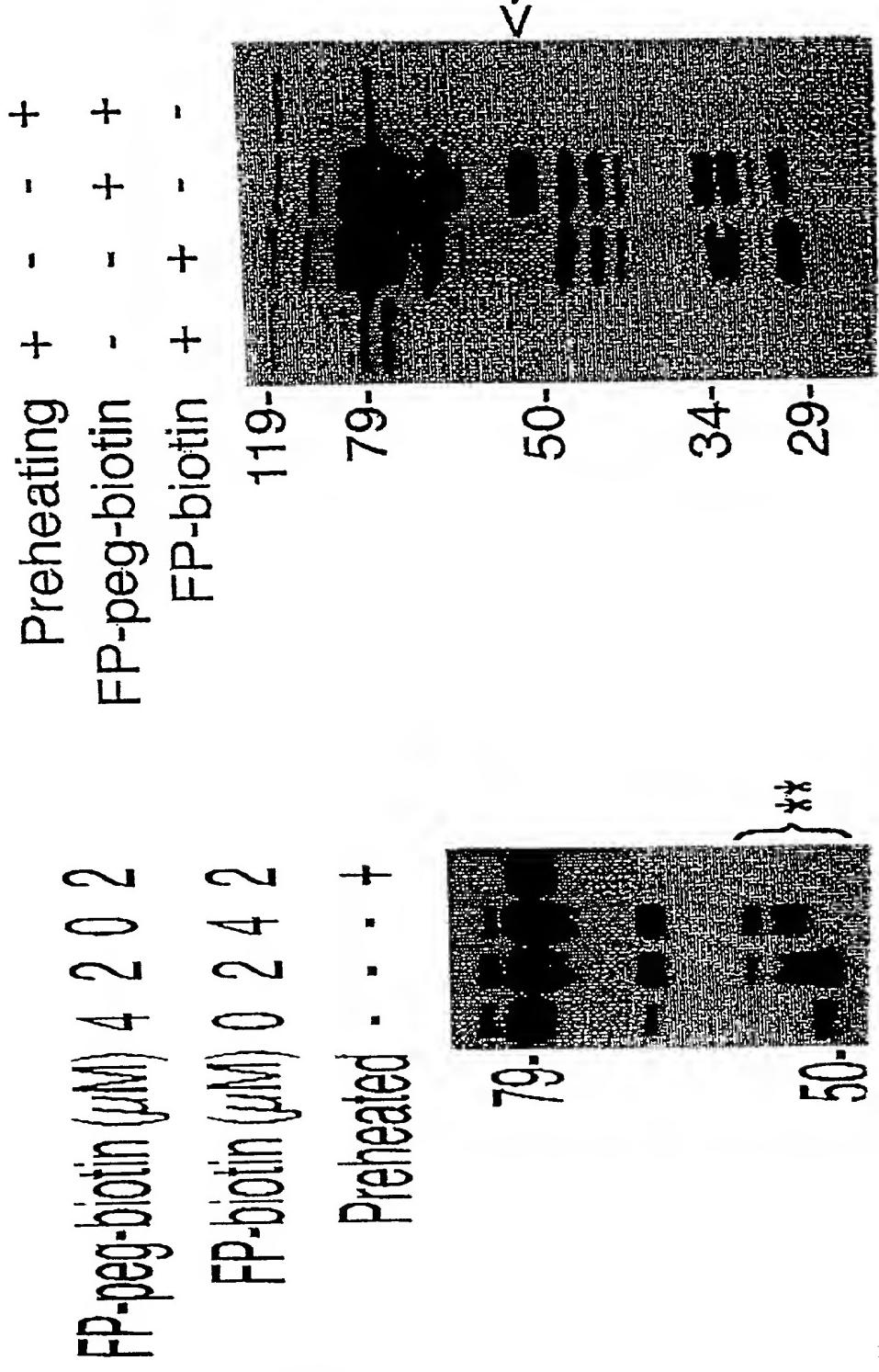


FIGURE 6

FIGURE 7

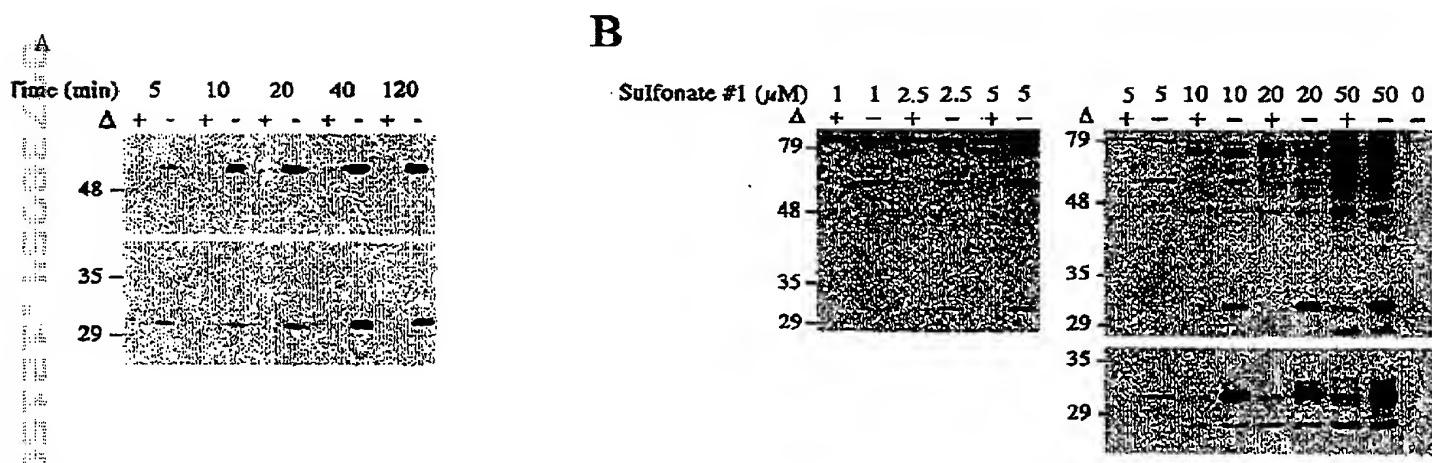
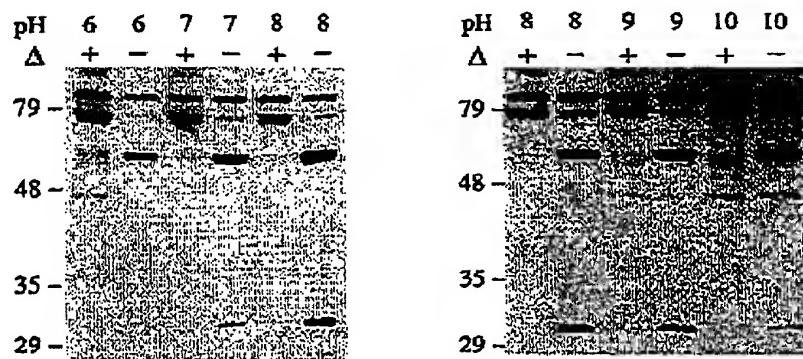


FIGURE 7

C



D

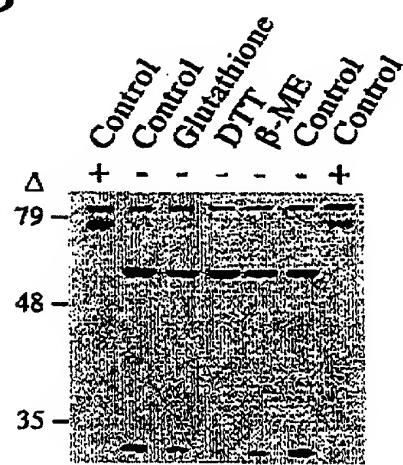


FIGURE 8

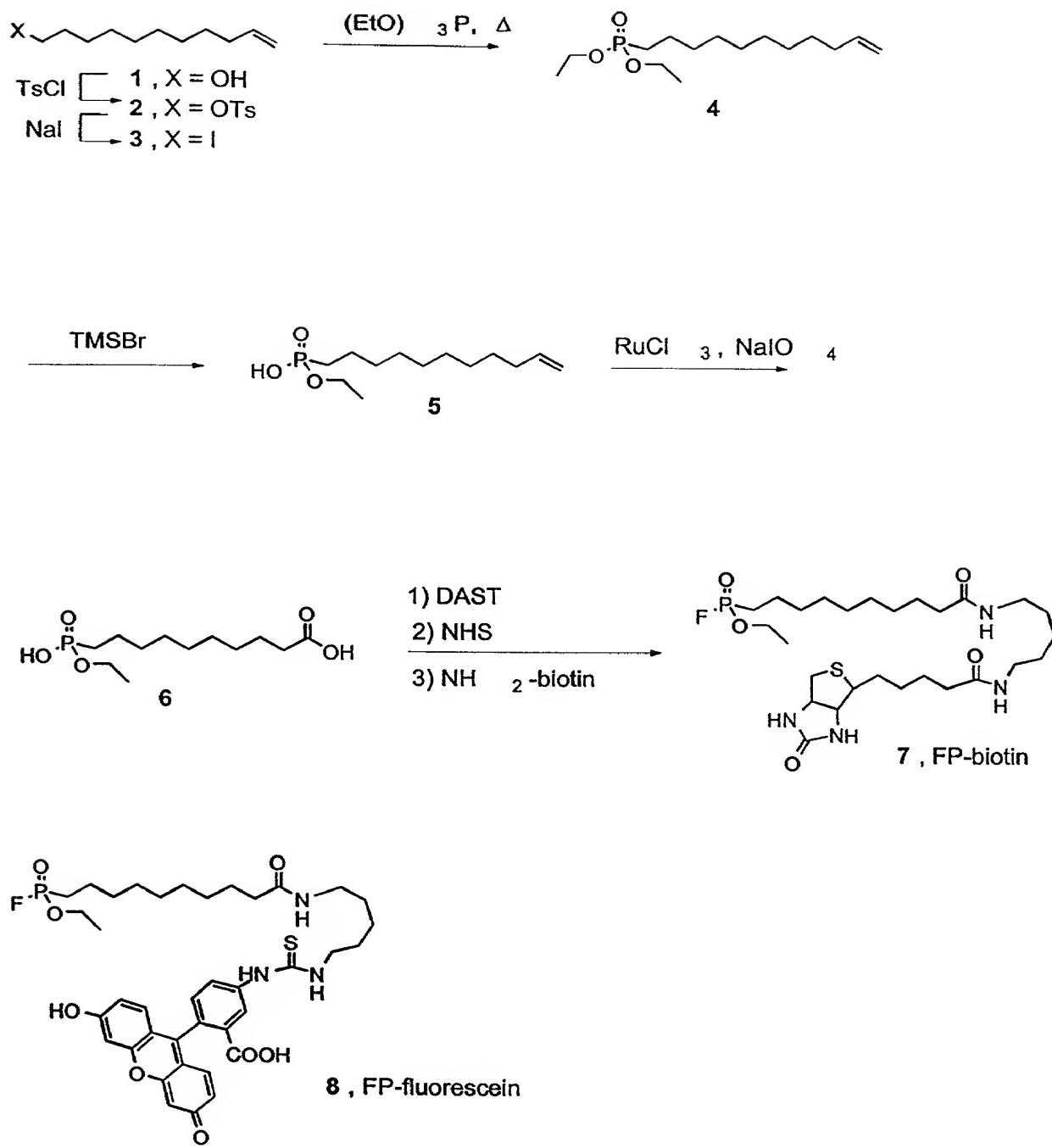


FIGURE 9

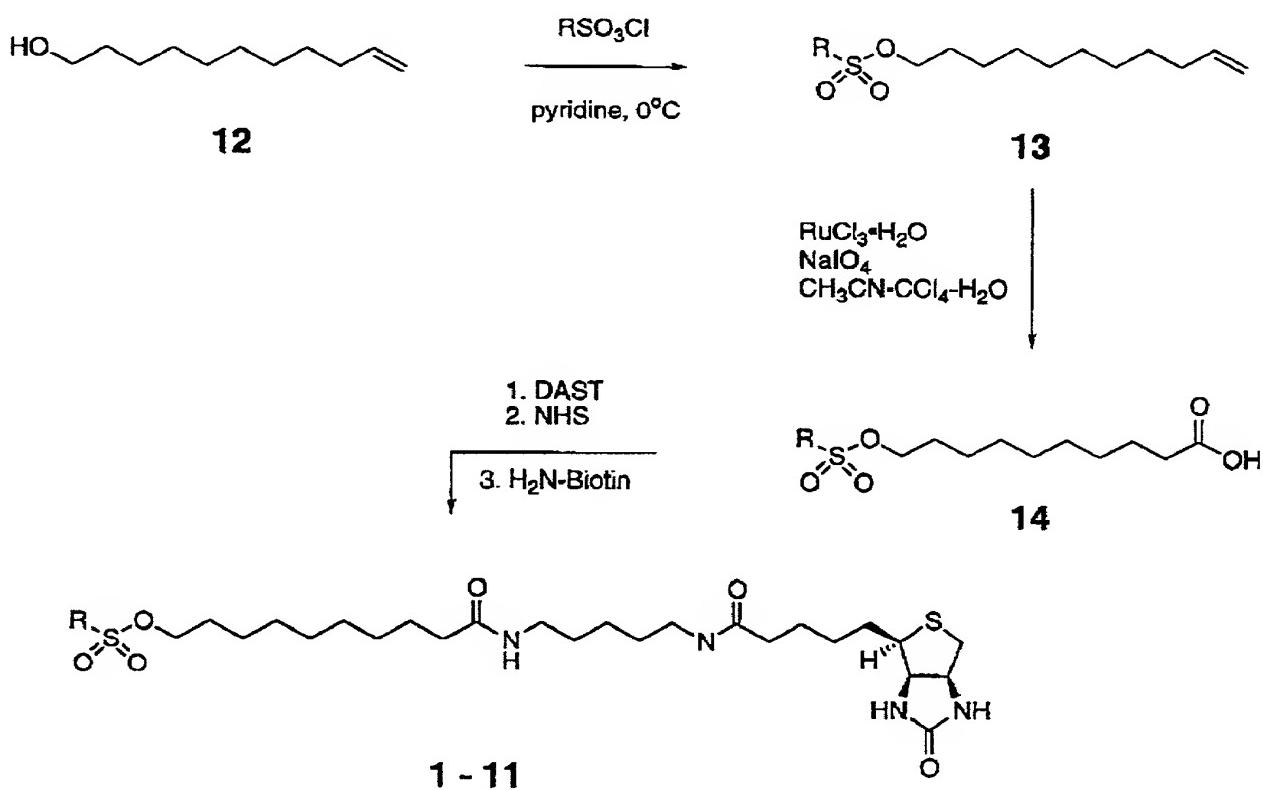
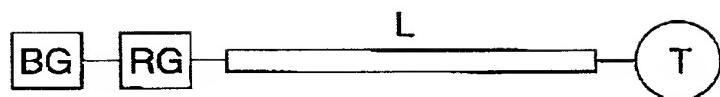


FIGURE 10

A.



B.

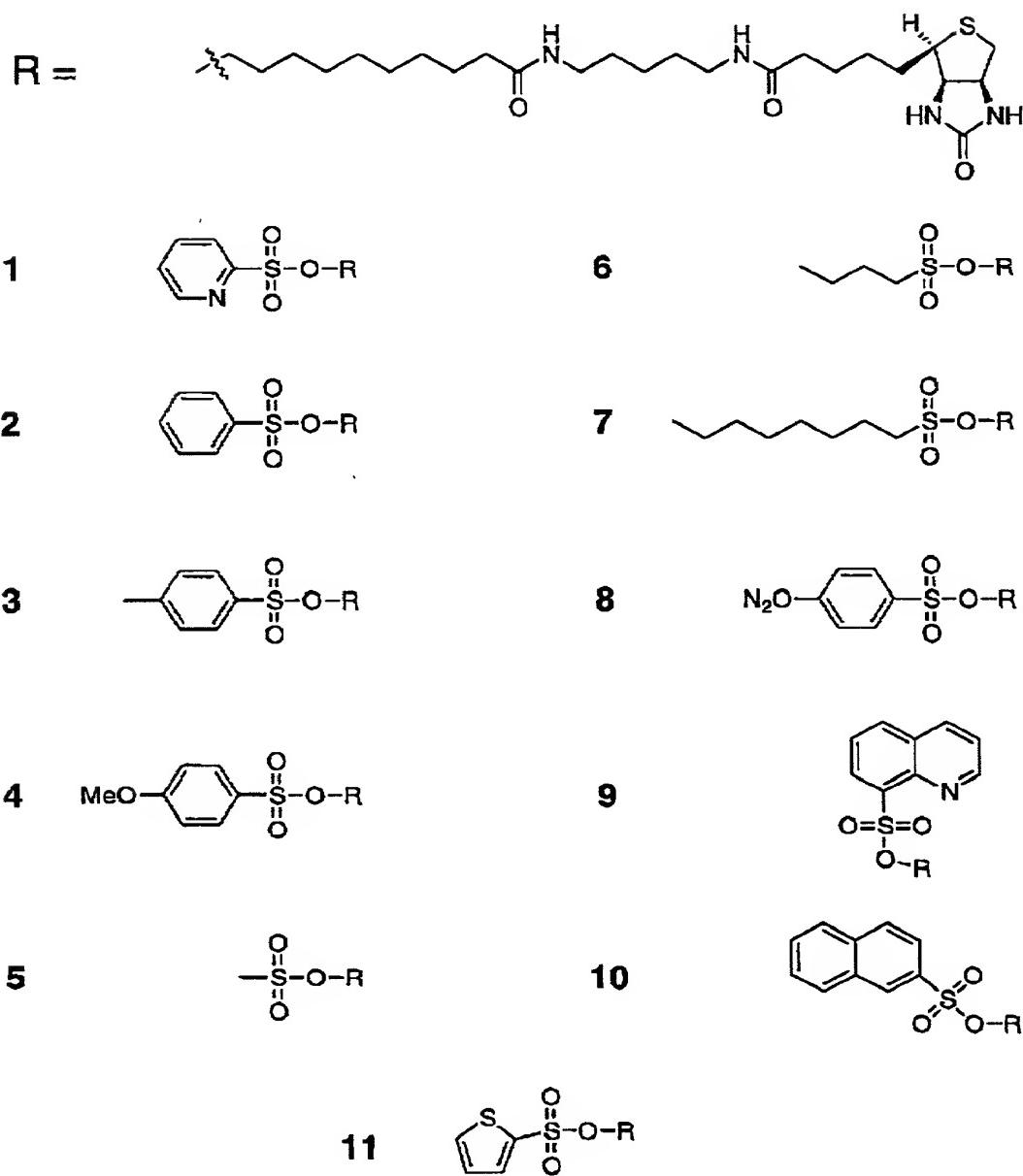
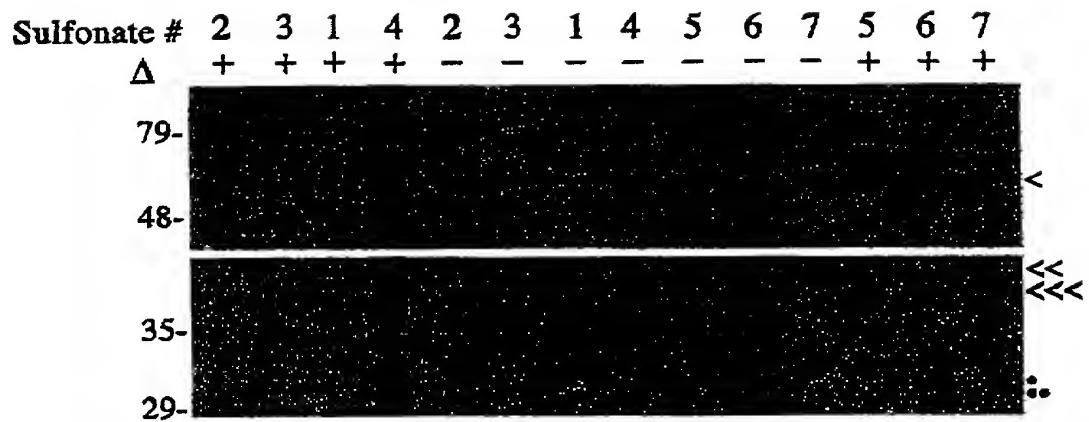


FIGURE 11

A



B

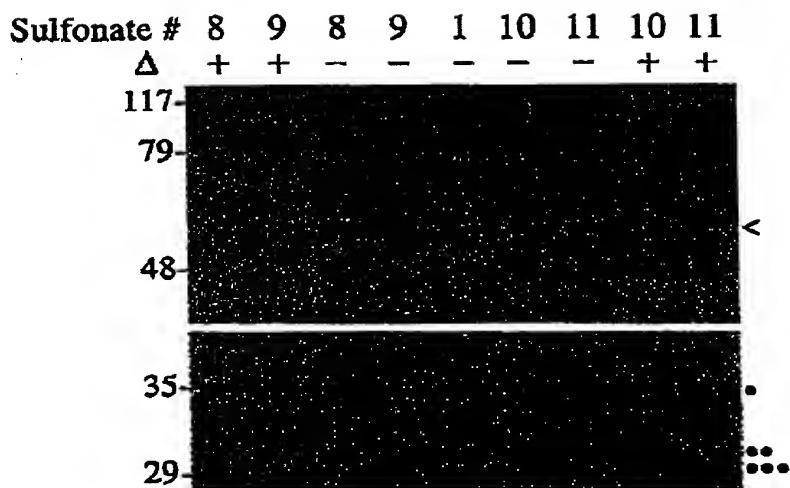


FIGURE 12

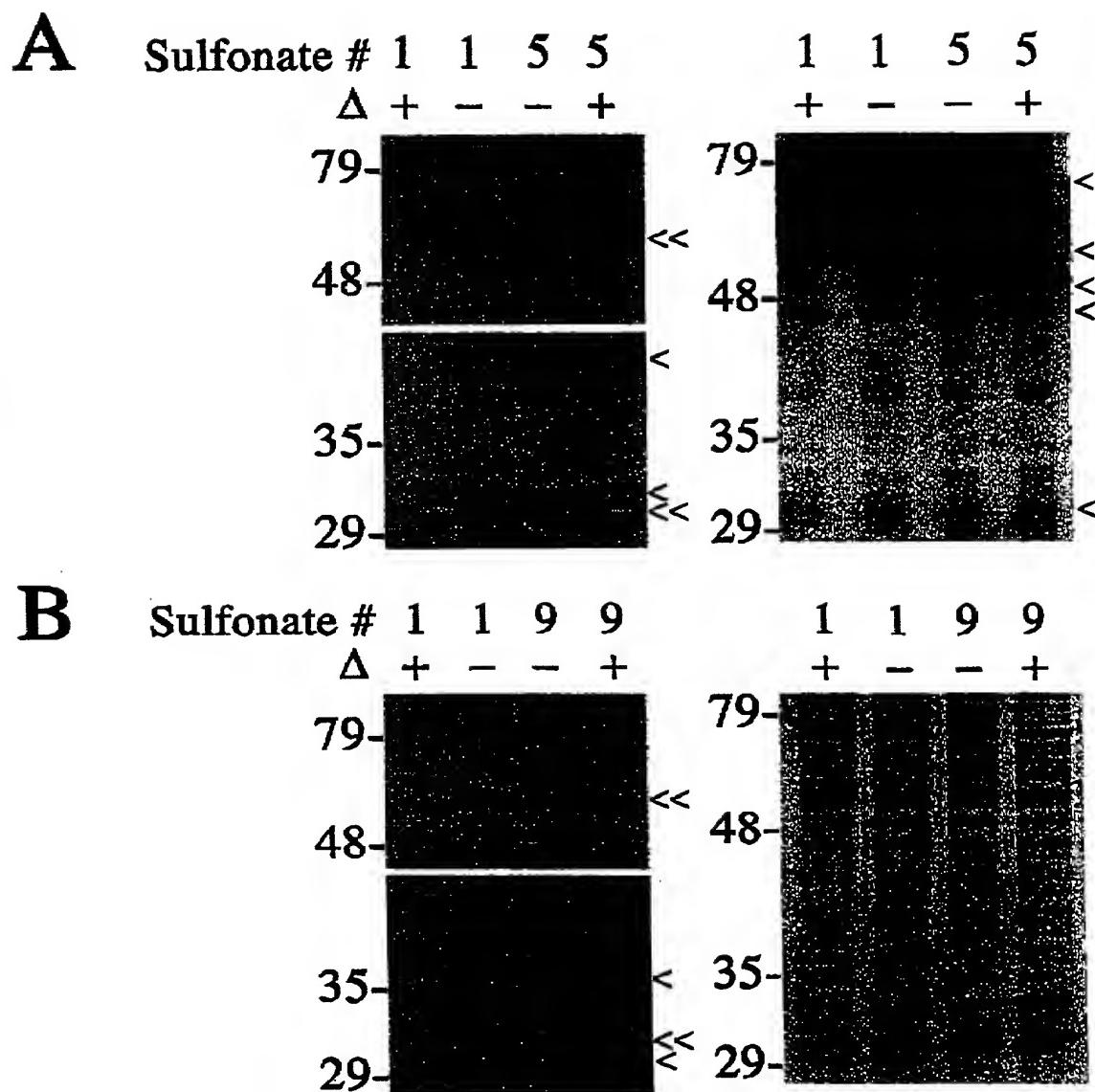


FIGURE 13

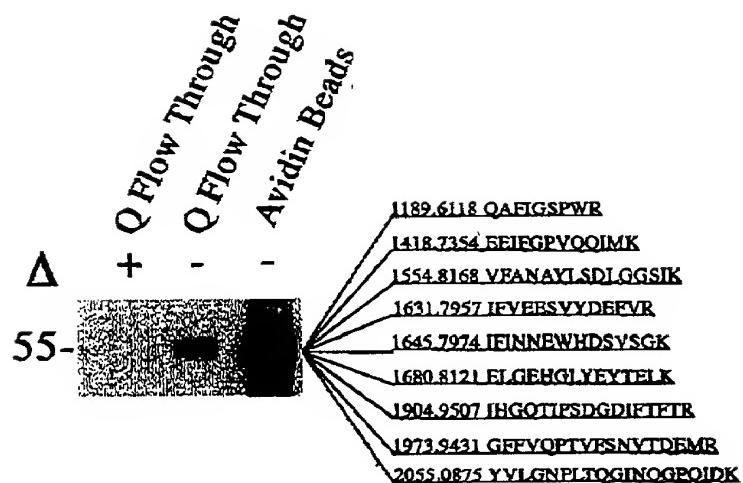
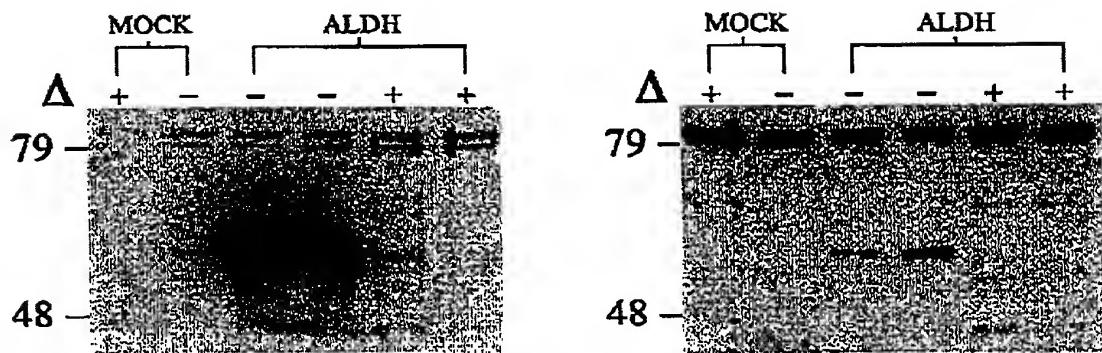
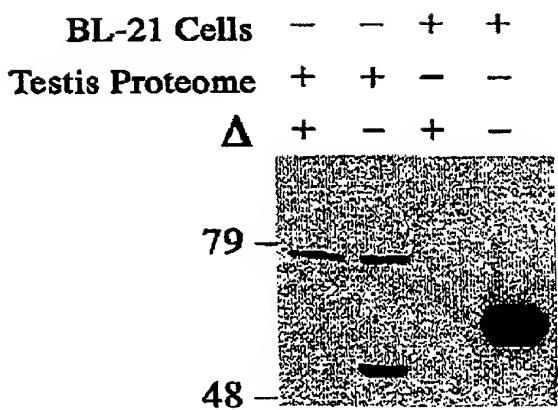
A**B****C**

FIGURE 14

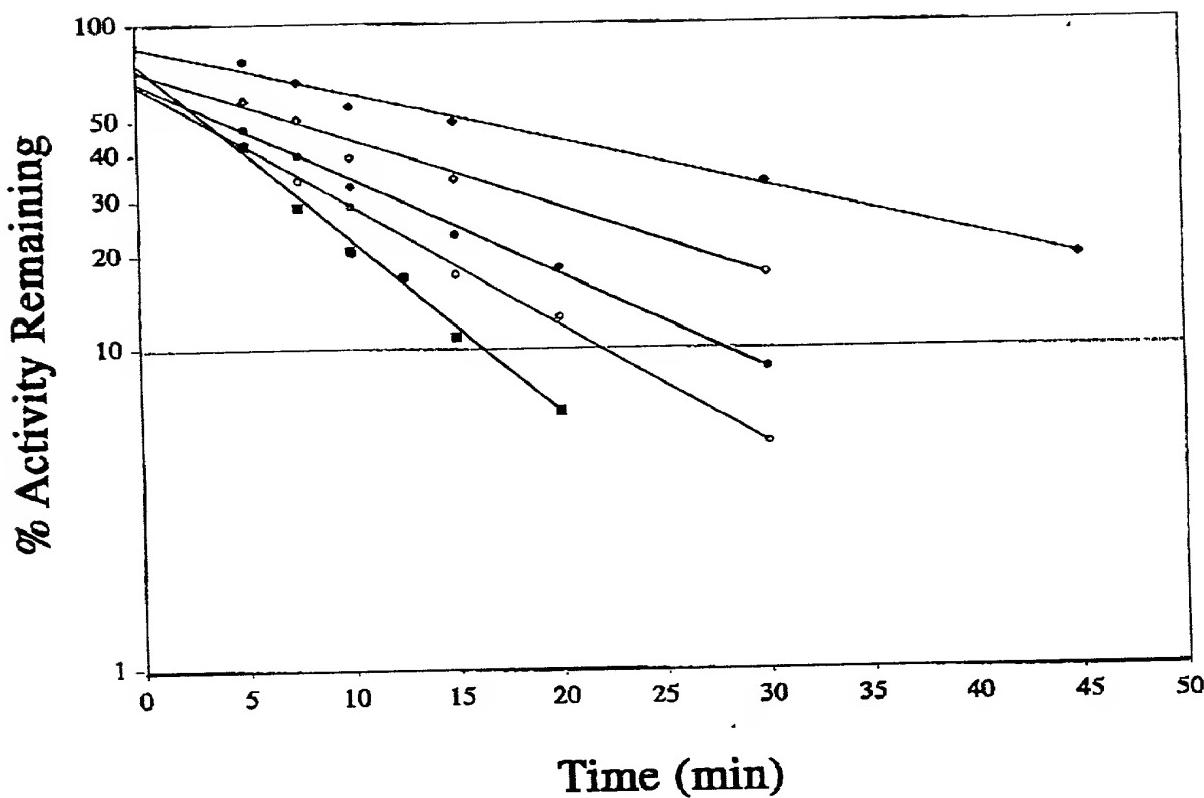
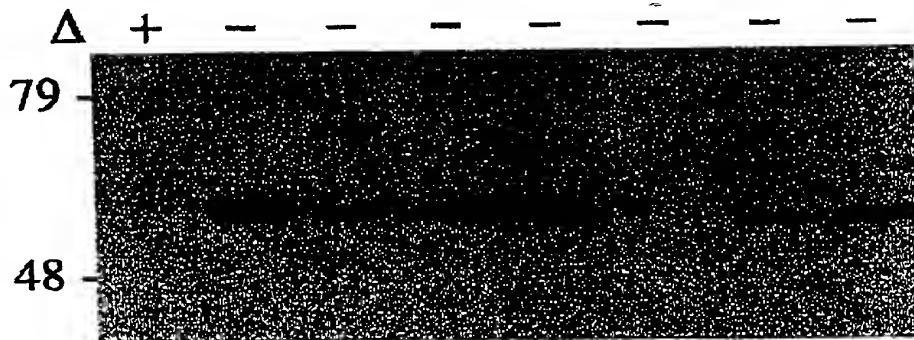
A**B**
Competitor # - - 15 17 16 15 17 16
[Competitor (μ M)] 0 0 5 5 5 50 50 50
 Δ + - - - - - - -

FIGURE 15

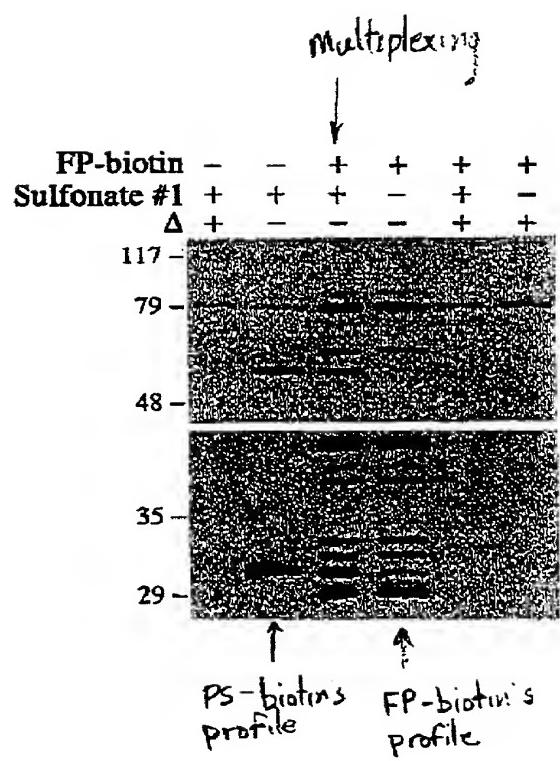


FIGURE 16

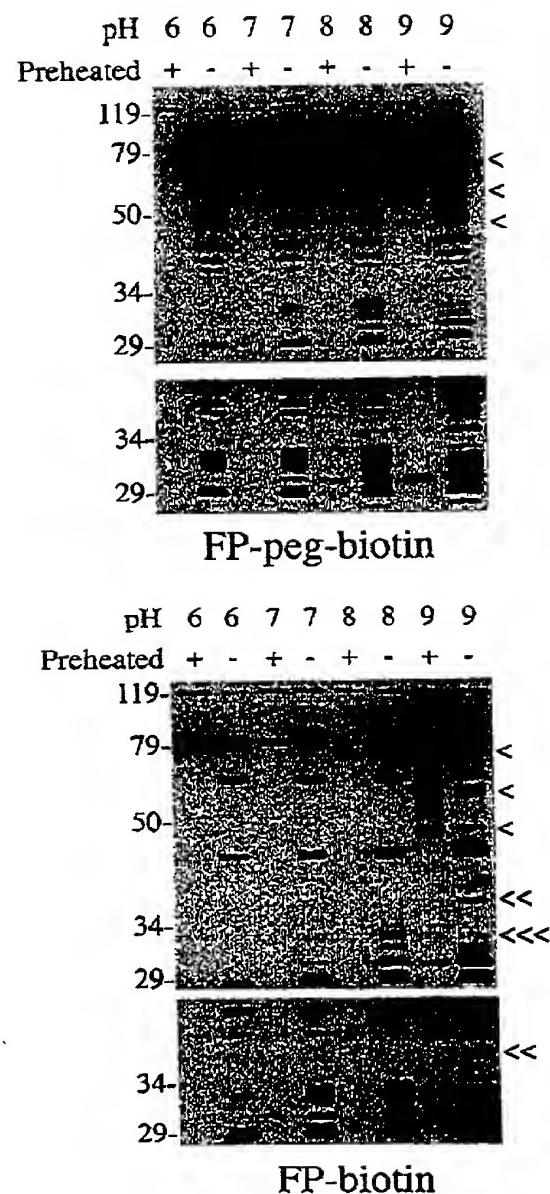


FIGURE 17

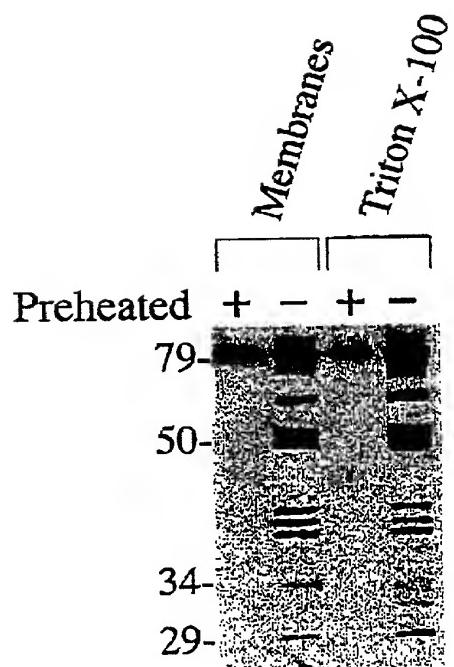


FIGURE 18

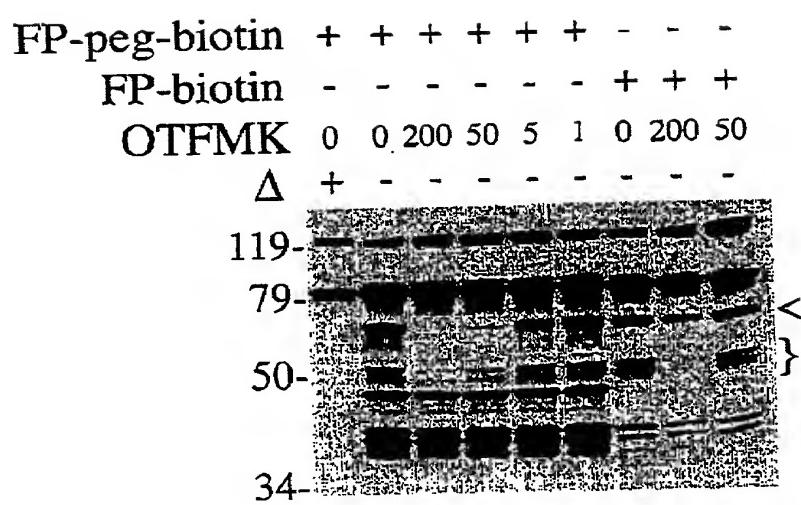


FIGURE 19

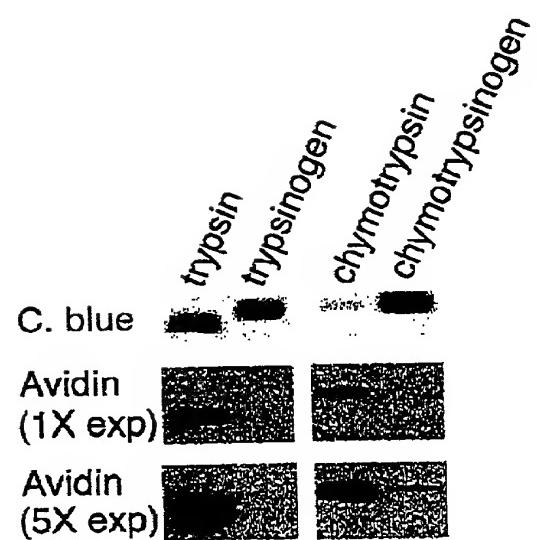


FIGURE 20

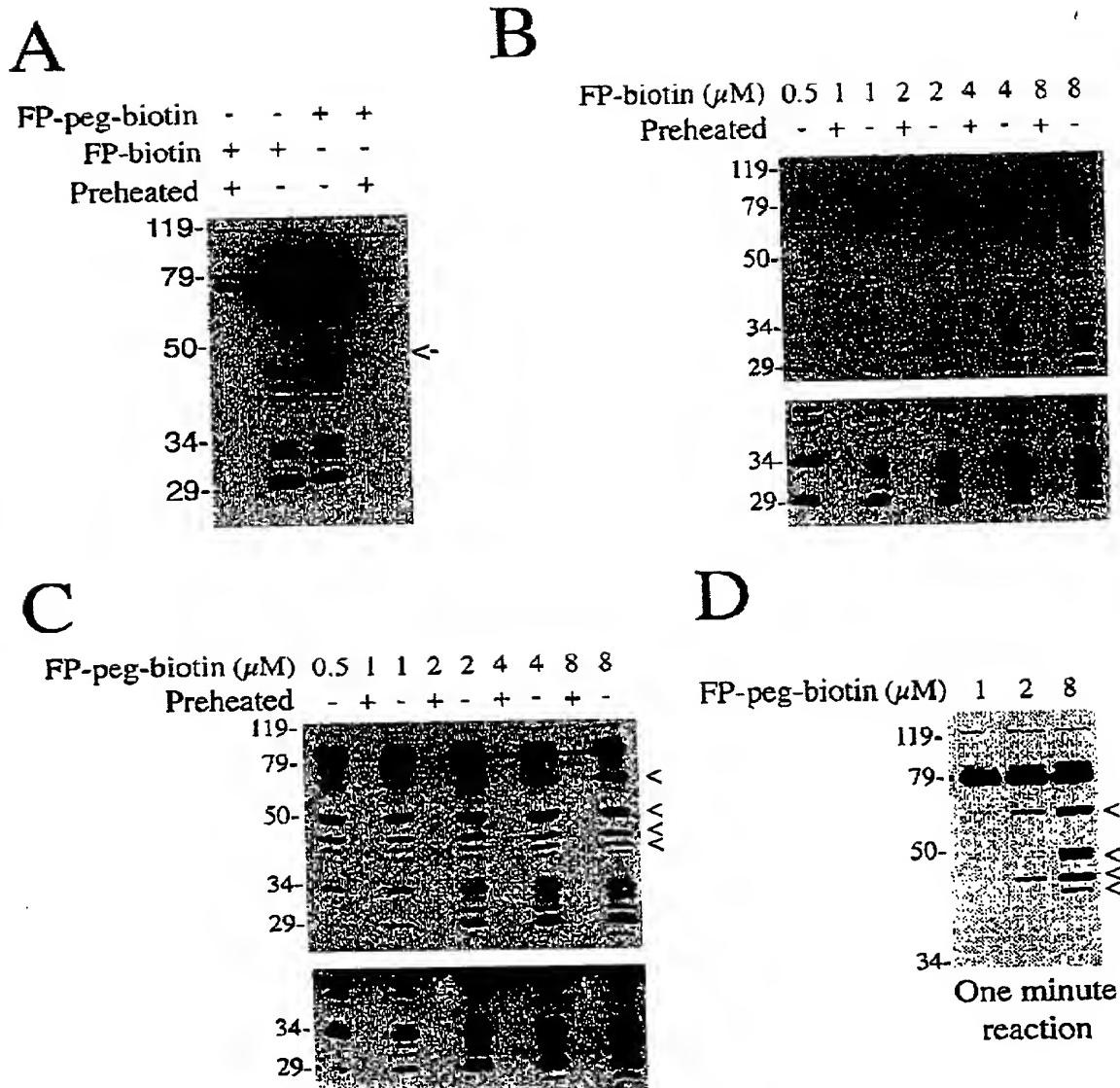


FIGURE 21

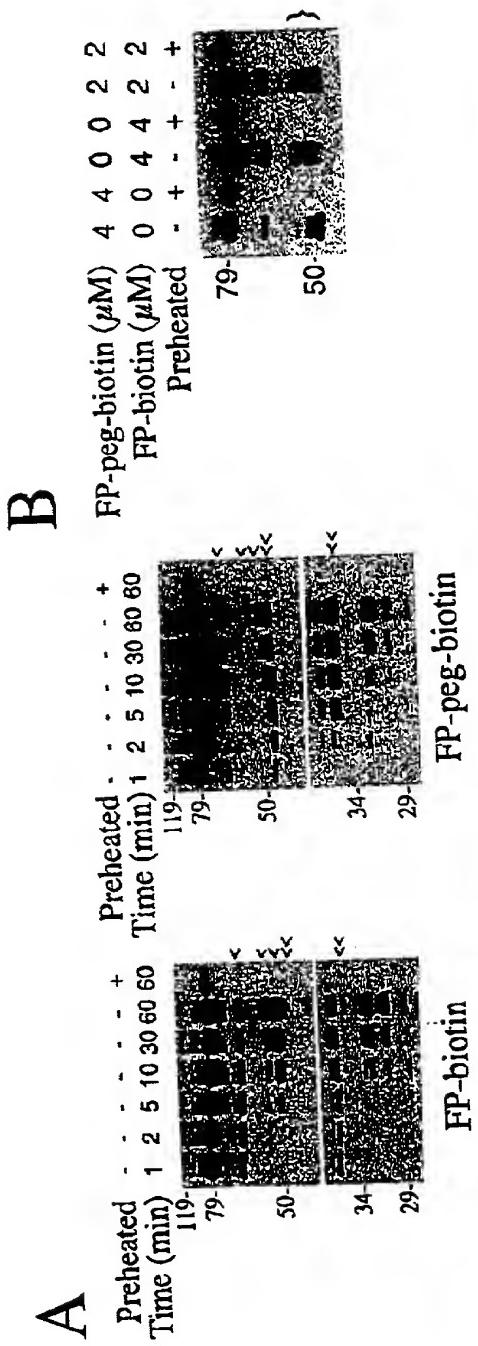


FIGURE 22

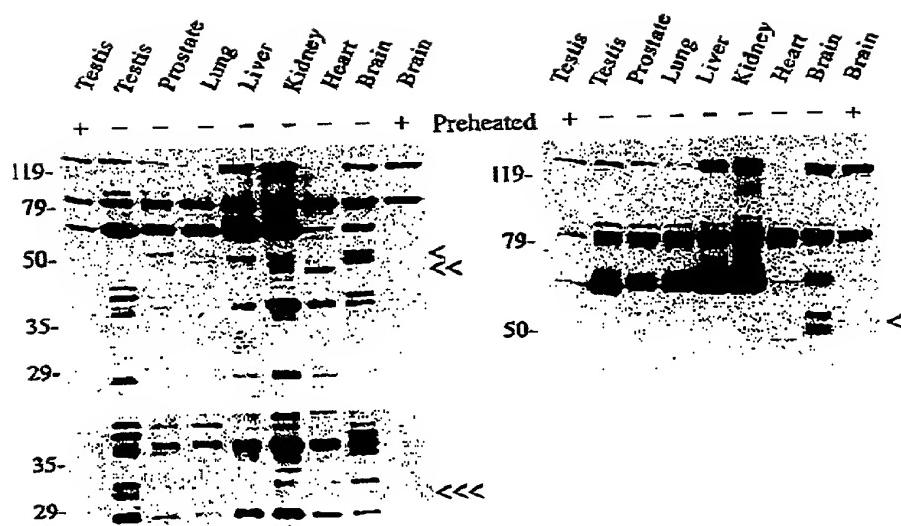


FIGURE 23

